Emerging Resistance to Quinolones Among *Salmonella* Typhi Isolates in the United States, 1999-2001

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Background: Each year an estimated 800 persons in the United States are infected with *Salmonella* Typhi. Effective antimicrobial treatment, now commonly with ciprofloxacin (a fluoroquinolone), has reduced mortality from 20% to less than 1%. Resistance to nalidixic acid (a quinolone) is correlated with decreased susceptibility to ciprofloxacin (MIC $\geq$ 0.12µg/ml); recent evidence suggests that patients infected with *Salmonella* Typhi with decreased susceptibility to ciprofloxacin respond poorly to therapy.

Methods: Since 1999, state and local public health laboratories participating in the National Antimicrobial Resistance Monitoring System submit *Salmonella* Typhi isolates received from clinical laboratories to the Centers for Disease Control and Prevention (CDC). At CDC, susceptibility testing to nalidixic acid and ciprofloxacin is performed by broth microdilution (Sensititre®).

Results: From 1999-2001, 554 *S*. Typhi isolates were tested and 135 (24%) were resistant to nalidixic acid; 2001 data are preliminary. Although no isolates were resistant to ciprofloxacin (MIC = 4µg/ml), 130 (96%) of nalidixic acid-resistant isolates had decreased susceptibility to ciprofloxacin. Nalidixic acid resistance increased from 19% (31/166) in 1999 to 30% (63/211) in 2001. Of 124 patients from whom nalidixic acid-resistant *Salmonella* Typhi was isolated and clinical information complete, 96 (77%) isolates were from blood, 51 (41%) patients were female and the median age of patients was 22.5 years (range 1-75).

Conclusions: Clinicians should be aware that a high proportion of *Salmonella* Typhi isolates in the United States are resistant to nalidixic acid, which may portend clinical fluoroquinolone failure. Continued laboratory surveillance is essential to track emerging resistance. Correlation of in-vitro susceptibility and clinical outcomes will be required to inform decisions about breakpoints for ciprofloxacin and guidelines regarding appropriate empirical treatment for typhoid fever.

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